I. Scientific Abstract

This is a phase I trial to evaluate DNA vaccination in patients with high risk melanoma. The objective of this study is to determine the safety and immunogenicity of vaccination with the genes coding for mouse and human gp100 in patients with AJCC stage IIB, IIC, III and IV melanoma who are HLA-A2+. We will assess whether DNA vaccination is safe and generates an immune response to an otherwise poorly immunogenic melanoma differentiation antigen.

The hypothesis that xenogeneic DNA encoding a homologous antigen is more potent than syngeneic DNA encoding a tumor antigen will be tested. A randomized crossover design of a phase I study will be used to assess this hypothesis. We will assess two closely related DNA vaccines against gp100. Studies in animal models have demonstrated that xenogeneic DNA (i.e., homologous DNA from a different species) can be more potent in inducing antibody and T cell responses against melanoma differentiation antigens than vaccination with self DNA. Patients will be randomly assigned to vaccination with either xenogeneic (mouse) or human gp100 DNA delivered intramuscularly at three different dose levels (100, 500, or 1500 μg in divided doses) every three weeks for three immunizations. Following this initial vaccination period, those patients previously randomized to receive mouse gp100 DNA will receive three immunizations with human gp100 DNA at three week intervals. Likewise, those patients initially randomized to receive human gp100 DNA will then receive three immunizations with mouse gp100 DNA at three week intervals. If patients have stable or clinically responding disease, additional vaccinations are administered bimonthly for up to four additional vaccinations. A total of at least 18 patients will be enrolled. Patients' sera and peripheral blood mononuclear cells will be collected in order to measure the antibody and T cell responses induced by the vaccines. Specifically, titers of IgM and IgG antibodies against human and mouse gp100 will be measured for serological response and Elispot assays for CD8+ T cells responses will be assessed.